

Application No: 10/568, 332
October 15, 2010

AMENDMENTS TO THE CLAIMS:

Claims 1-12 (Cancelled).

Claim 13 (Previously Presented). A process for the preparation of a recombinant interferon alpha 2, comprising:

(a) obtaining a crude preparation of a recombinant interferon alpha 2,

wherein the crude preparation of the recombinant interferon alpha 2 is obtained by a process comprising:

(i) fermentation of a prokaryotic host cell comprising a periplasm and being transformed with a recombinant expression system capable of bringing about secretion of a recombinant interferon alpha 2 into the periplasm of said host cell, wherein said fermentation is performed in a fermentation medium under conditions such that the recombinant interferon alpha 2 is secreted into the periplasm, and

(ii) extraction of the recombinant interferon alpha 2 from the periplasm by applying an osmotic shock to the host cells contained in the fermentation medium; and

(b) applying the crude preparation to a multi-step chromatography comprising the following steps in sequence:

- (i) cation exchange chromatography,
- (ii) anion exchange chromatography,
- (iii) hydrophobic interaction chromatography,
- (iv) cation exchange chromatography, and
- (v) size exclusion chromatography.

Claim 14 (Cancelled).

Claim 15 (Previously Presented). The process according to claim 13, wherein said osmotic shock is performed by adding an agent to the fermentation medium, and subsequently diluted with water, wherein the agent is selected from the group consisting of sucrose, sodium chloride, arginine, lysine, guanidine hydrochloride, Triton-X 100, polyethyleneimine, and

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suitable mixtures of one or more thereof, and wherein said agent, after dilution with H₂O, creates an osmotic pressure leading to disruption of the outer cell membrane of the host cell.

Claim 16 (Cancelled).

Claim 17 (Original). The process according to claim 15, wherein said agent is sucrose.

Claim 18 (Original). The process according to claim 17, wherein the concentration of the sucrose in the fermentation medium when starting the dilution is about 20% weight/volume.

Claim 19 (Original). The process according to claim 18, wherein the dilution factor of the sucrose-containing fermentation broth with H₂O is at least about 3 times.

Claim 20 (Previously Presented). The process according to claim 24, wherein said prokaryotic host cell is a Gram-negative bacterium.

Claim 21 (Original). The process according to claim 20, wherein said Gram-negative bacterium is selected from the group consisting of Escherichia coli, Pseudomonas sp., Enterobacter sp., Campylobacter sp. and Vitreoscilla sp.

Claim 22 (Original). The process according to claim 20, wherein the Gram-negative bacterium is E. coli.

Claim 23 (Original). The process according to claim 13, wherein said interferon alpha 2 is selected from the group consisting of interferon alpha 2A and interferon alpha 2B.

Claim 24 (Previously Presented). The process according to claim 13, wherein said crude preparation is obtained from a prokaryotic host cell expressing said recombinant interferon alpha 2.

Claim 25 (Cancelled).